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Critical determinants of combined sprint and endurance performance: an integrative analysis from muscle fiber to the human body

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ABSTRACT: Optimizing physical performance is a major goal in current physiology. However, basic understanding of combining high sprint and endurance performance is currently lacking. This study identifies critical determinants of combined sprint and endurance performance using multiple regression analyses of physiologic determinants at different biologic levels. Cyclists, including 6 international sprint, 8 team pursuit, and 14 road cyclists, completed a Wingate test and 15-km time trial to obtain sprint and endurance performance results, respectively. Performance was normalized to lean body mass$^{2/3}$ to eliminate the influence of body size. Performance determinants were obtained from whole-body oxygen consumption, blood sampling, knee-extensor maximal force, muscle oxygenation, whole-muscle morphology, and muscle fiber histochemistry of musculus vastus lateralis. Normalized sprint performance was explained by percentage of fast-type fibers and muscle volume ($R^2 = 0.65$; $P < 0.001$) and normalized endurance performance by performance oxygen consumption ($\dot{V}o_2$), mean corpuscular hemoglobin concentration, and muscle oxygenation ($R^2 = 0.92$; $P < 0.001$). Combined sprint and endurance performance was explained by gross efficiency, performance $\dot{V}o_2$, and likely by muscle volume and fascicle length ($P = 0.056$; $P = 0.059$). High performance $\dot{V}o_2$ related to a high oxidative capacity, high capillarization × myoglobin, and small physiologic cross-sectional area ($R^2 = 0.67$; $P < 0.001$). Results suggest that fascicle length and capillarization are important targets for training to optimize sprint and endurance performance simultaneously.—Van der Zwaard, S., van der Laarse, W. J., Weide, G., Bloemers, F. W., Hofmijster, M. J., Levels, K., Noordhof, D. A., de Koning, J. J., de Ruiter, C. J., Jaspers, R. T. Critical determinants of combined sprint and endurance performance: an integrative analysis from muscle fiber to the human body. FASEB J. 32, 2110–2123 (2018). www.fasebj.org

KEY WORDS: skeletal muscle · oxidative capacity · oxygen transport · muscle architecture · muscle biopsy

Many sports require a combination of sprint and endurance performance. During the past decades, physiologic determinants of physical performance have been the subject of intensive investigation (*e.g.*, in cycling, 1–11). Studies focused on determinants of either sprint (*e.g.*, 8–18) or endurance performance (*e.g.*, 1–7, 19–23), even though physical performance is rarely a dichotomous function of only sprint or only endurance. Generally, a limited number of whole-body determinants of sprint or endurance performance have been studied, although there are many physical performance determinants at different levels (*i.e.*, molecular, cellular, whole-muscle, organ, and whole

ABBREVIATIONS: 3D, 3-dimensional; CAF, capillaries around the fiber; CD, capillary density; C/F, capillary-to-fiber ratio; FCSA, fiber cross-sectional area; f$\dot{V}o_{2max}$, fiber maximal oxygen consumption; [Hb], hemoglobin concentration; Hct, hematocrit; [HHbMb], deoxygenated hemoglobin and myoglobin concentration; iSDH activity, spatially integrated SDH activity, SDH activity × FCSA; KE, knee-extension; LBM, lean body mass; L_f, fascicle length; LT1/2, first/second lactate threshold; [Mb], myoglobin concentration; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; MHC, myosin heavy chain; [O_2HbMb], oxygenated hemoglobin and myoglobin concentration; PCSA, muscle physiological cross-sectional area; performance $\dot{V}o_2$, average oxygen consumption during the 15-km time trial; PO_2, oxygen tension; PO_{peak}, peak power output; $PO_{peak} + PO_{TT}$, combined sprint and endurance performance; PO_{TT}, average power output during a 15-km time trial; RBC, red blood cell; SDH, succinate dehydrogenase; UEA-1, *Ulex europaeus* agglutinin 1 lectin; VL, *vastus lateralis*; $\dot{V}o_{2max}$, maximal oxygen consumption, $VT_{1/2}$, first/second ventilatory threshold; W_{max}, maximum workload

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body), which may interact. This increases the complexity of maximizing performance and increases the complexity of physiologic adaptations in response to training and/or nutritional interventions. So far, most research has addressed determinants of physical performance at the organ or whole-body level (*e.g.*, in cycling, 1–11). Another factor that adds to the complexity of optimizing physical performance is that adaptations for endurance or peak power are mutually exclusive, particularly in skeletal muscle (24–26).

Prime determinants of physical performance in humans are skeletal muscle endurance and maximal power-generating capacity (25, 27). Muscle peak power is largely determined by the myosin heavy chain isoform expression and muscle volume (*e.g.*, 11, 12, 16–18, 28–31), whereas (muscle) endurance capacity relies on mitochondrial oxidative capacity and oxygen supply toward and within the muscle (*e.g.*, 1, 20–22, 27, 32–34). It is, however, generally acknowledged that muscle fiber size and oxidative capacity are inversely related (25, 35). Apparently, these are adapted such that oxygen demand and supply are matched and that muscle fibers prevent hypoxia at maximal oxygen consumption ($\dot{V}o_{2max}$) (25, 36). Increasing both fiber size and oxidative capacity is commonly endeavored in sports and rehabilitation training, but with limited success (24). Moreover, molecular signaling pathways for mitochondrial biogenesis inhibit contractile muscle protein synthesis (24–26). Improving both traits simultaneously is, therefore, highly challenging. It has been postulated that, to increase both fiber size and oxidative capacity, one should enhance oxygen supply toward and within the muscle fibers (25). That should accommodate the increased oxygen diffusion distance from capillaries to the mitochondria, resulting from increases in fiber size (25). Given the interference among determinants for peak power and endurance performance, the question arises how to improve both traits simultaneously.

An integrative approach assessing how physiologic determinants are related to performance of top-level athletes may provide new insights in the key determinants and the most optimal combination of determinants for combined sprint and endurance performance. For this purpose, we assessed the critical determinants of sprint, endurance, and combined sprint and endurance performance in athletes using the explained variance by correlation and multiple regression analyses. We assessed sprint performance by peak power production and the following determinants: muscle fiber size, muscle fiber type, number of muscle fibers, and whole-muscle morphology of *musculus vastus lateralis* (VL), blood lactate concentration, maximal isometric torque, and specific force. Endurance performance was assessed during a time trial with determinants: muscle fiber oxidative capacity, muscle fiber type, oxygen supply toward muscle fiber (reflected by capillaries and blood parameters) and within muscle fiber [reflected by myoglobin concentration (Mb)], whole-muscle oxygenation of VL, blood lactate concentration, whole-body oxygen consumption, and mechanical gross efficiency. Maximal power of an organism is scaled to its body size. To eliminate effects of body size and to investigate only biologic differences in power production, physical performance was normalized to lean body mass (LBM). Cross-sectional studies among cyclists are likely a useful model to investigate critical determinants of combined sprint and endurance performance because cycling disciplines focus on either optimization of sprint, endurance, or on both sprint and endurance (38). We assessed determinants of combined sprint and endurance performance in sprint, team pursuit, and road cyclists because those cyclists were expected to have optimized physical performance within their respective cycling discipline.

MATERIALS AND METHODS

Subjects

Included in the study were 28 cyclists (14 road, 8 team pursuit, and 6 track sprint). Cyclists [means ± SD: age, 25 ± 7 yr; weight, 77.4 ± 8.1 kg; height, 1.86 ± 0.06 m, body–mass index, 22.4 ± 1.9; lean body mass, 68.8 ± 6.0 kg; $\dot{V}o_{2max}$, 62.7 ± 7.9 ml/kg/min, as previously described (34)] competed at the national, international, or Olympic level, except for 4 amateur road cyclists. The study was conducted according to the Declaration of Helsinki (2013) and was approved by the VU Medical Center Ethics Committee (NL49060.029.14). Subjects provided written, informed consent and were instructed to avoid strenuous exercise and alcohol consumption (<24 h) and to consume no meals and caffeinated beverages (<3 h) before exercise testing. Training specifics are described in Supplemental Data S1.

Whole-body cycling performance

For sprint performance, 1-s peak power output (PO_{peak}) was obtained from a 30-s Wingate test on a bicycle ergometer (Monark 894 E Peak Bike; Monark Exercise, Vansbro, Sweden). Subjects received strong verbal encouragement and remained seated throughout the test. Workload was applied after 2 revolutions and was set at 10% body mass; 1 min after exercise, blood lactate concentration was obtained from the fingertip (Lactate Pro 2; Arkray KDK, Kyoto, Japan). For endurance performance, we obtained average power output during a 15-km time trial (PO_{TT}) on an electronically braked bicycle ergometer (VU-MTO, Amsterdam, The Netherlands). Power output was determined from torque and cadence measurements sampled at 100 Hz. Completed cycling distance was calculated as a function of power output, rolling friction ($\mu_r = 0.003$) and air friction ($\mu_a = 0.17$), similar to road cycling. Subjects self-selected their preferred gear ratio and received visual and verbal feedback on their time trial progression.

To eliminate the influence of body size and to investigate only biologic differences in power production (rather than physical principles), physical performance was normalized to $LBM^{2/3}$ (37). Fat mass was obtained from the sum of 4 skin folds (39).

How well individual cyclists were able to combine sprint and endurance performance was expressed relative to the whole group. Combined sprint and endurance performance (PO_{peak} + PO_{TT}) was assessed by perpendicular residuals to the Deming regression line between PO_{TT} and PO_{peak}, that is, the perpendicular projections of the data points onto that regression line as seen in Fig. 2. Thus, perpendicular residuals equal the perpendicular distances from individual data points to the Deming regression line, which accounts for an error in both variables, instead of error in variable y only. Those residuals quantify both

how much a cyclist's sprint performance differs from his expected sprint performance (*i.e.*, δ between actual sprint performance and predicted sprint performance based on the regression line and the cyclist's actual endurance performance) as well as how much endurance performance differs from the cyclists expected endurance performance (*i.e.*, δ between actual endurance performance and predicted endurance performance based on the regression line and cyclist's actual sprint performance).

Whole-body oxygen consumption

Whole-body $\dot{V}o_2$ was obtained during the 15-km time trial and during a maximal incremental exercise test (on a Monark Ergomedic 839E; Monark Exercise), and was recorded breath-by-breath using open circuit spirometry (Cosmed Quark CPET; Cosmed, Rome, Italy). Before testing, gas analyzer and volume transducer were calibrated according to manufacturer's instructions. Breath-by-breath data were smoothed and then averaged over the time trial to obtain performance $\dot{V}o_2$. $\dot{V}o_{2max}$ was calculated as the highest 30-s value and maximum workload (W_{max}) as the highest 3-min value achieved during the maximum-effort incremental test to voluntary exhaustion. Initial workload was 80 W and increased by 40 W/3 min. Gross efficiency was calculated for the last minute of each increment, dividing mechanical power by oxidative metabolic power and accounting for power loss within the Monark transmission system (2). Metabolic power was derived from $\dot{V}o_2$ and respiratory exchange ratio (40). Highest gross efficiency was obtained with respiratory exchange ratio < 1.0 and $\dot{V}o_2$ in steady state [$<5\%$ change between min 2 and 3 of each increment (40)]. $\dot{V}o_2$ at ventilatory thresholds (VT_1 and VT_2) and lactate thresholds (LT_1 and LT_2) were obtained from 30-s moving averages. VT_1 was determined using the V-slope method and ventilatory equivalents (41), and VT_2 was derived from minute ventilation *vs.* $\dot{V}co_2$ plots and ventilatory equivalents (42). Blood lactate concentration was obtained at the end of each incremental step, and values were linearly interpolated to retrieve LT1 at a blood lactate of 2 mM and LT_2 at 4 mM (43). $\dot{V}o_2$ and W_{max} values were also normalized to $LBM^{2/3}$.

Muscle oxygenation

Changes in deoxygenated hemoglobin + [Mb] ([HHbMb]) and oxygenated hemoglobin + [Mb] ([O_2HbMb]) were measured with respect to the start of the 15-km time trial, using a continuous-wavelength near-infrared spectroscopy device (Portamon; Artinis Medical Systems, Elst, The Netherlands), according to Van der Zwaard *et al.* (44).

Maximal isometric knee-extension torque

Maximal isometric knee-extension (KE) torque of the right leg was measured using a custom-made dynamometer. Active knee flexion angle was set at 60° during submaximal activation, after aligning the subject's anatomic knee axis with the dynamometer rotation axis, and hip flexion angle was set at 85° (full extension equals 0°). The lower leg was protected by a shin guard and strapped to a force transducer (KAP E/200 Hz; Bienfait, Haarlem, The Netherlands), placed 26.6 cm distally from the knee joint, and subjects were firmly secured with straps over hips and shoulders. After warm-up, subjects performed 4–5 attempts to attain maximal isometric KE torque, receiving online visual feedback on their force tracings. KE torque was obtained after multiplication of measured forces (sampled at 1 kHz) with the lever arm. Maximal isometric KE torque was calculated as highest 100-ms average obtained during the 5-s isometric contractions.

Whole-muscle morphology

Whole-muscle VL morphology was examined by 3-dimensional (3D) ultrasound (45). Briefly, the hip flexion angle was set at 85° and knee flexion angle at 60°. B-mode ultrasound images were collected at 25 Hz during multiple scans of the right VL using a 5-cm linear probe in longitudinal or transverse orientation (Technos MPX; Esaote, Firenze, Italy). Location and orientation of the probe were registered by a motion capture system (Optotrak Certus; Northern Digital, Waterloo, ON, Canada) and synchronized with ultrasound images to construct a 3D voxel array, using customized software (MatLab; MathWorks, Natick, MA, USA). Distal VL muscle belly end and proximal attachment to the trochanter major were identified by open-source, 3D image-processing software (Medical Imaging Interaction Toolkit; *http://www.mitk.org*). VL muscle volume was measured between these anatomic landmarks by manual segmentation of the anatomic cross-sections and subsequent interactive interpolation in medical imaging software. Fascicle length (L_f) and pennation angle between fascicle and distal aponeurosis (θ) were assessed within the midlongitudinal fascicle plane at a position two-thirds of the way along the muscle belly (distal from the origin). Physiologic cross-sectional area (PCSA) was calculated by dividing muscle volume by L_f. PCSA was multiplied by cosine θ to provide the effective PCSA (46).

Specific force of the VL was estimated using KE isometric torque, optimal patellar moment arm (d_{PT}), the contribution of VL to musculus quadriceps femoris and effective PCSA. The d_{PT} is very similar between subjects [means, 4.7–4.8 cm (46, 47)] and was assumed to be 4.75 cm in all cyclists. Because VL volume is ~34% of the total quadriceps femoris volume in cyclists (48), and that percentage is similar for PCSA and volume (47), VL specific force was estimated using Eq. 1:

$$\text{Specific force} = \frac{\text{KE torque} \times d_{PT}^{-1}}{0.34 \times \text{PCSA} \times \cos\theta} \quad (1)$$

Blood sampling

Resting blood samples were collected in EDTA-coated Vacutainer tubes (BD Biosciences, Franklin Lakes, NJ, USA) by venipuncture and analyzed for red blood cells (RBCs), hemoglobin concentration ([Hb]), hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC). Hct was determined by microhematocrit analysis.

Muscle biopsy samples

Biopsies were obtained from the right VL, as described previously (34). In brief, muscle biopsies were collected after local anesthesia ~15 cm above the patella at a depth of ~4 cm. Biopsy samples were aligned to muscle fiber arrangement, frozen in liquid nitrogen, and cut in 10-μm-thick sections using a cryostat at −20°C. Sections were collected on polylysine-coated slides and stored at −80°C until further analysis.

Muscle fiber histochemistry

Fiber-type composition was obtained by immunofluorescence analysis of myosin heavy chain (MHC) expression (49), using

primary antibodies BA-D5, SC-71, and 6H1 and secondary antibodies Alexa Fluor 488 IgG_{2b}, 488 IgG_1, and 647 IgM (all from Developmental Studies Hybridoma Bank, Iowa City, IA, USA). Fiber-type distribution (type I, I/IIA, IIA, IIAX, and IIX) was manually determined from 388 ± 142 fibers per subject (mean ± SD).

Mitochondrial oxidative capacity was assessed by succinate dehydrogenase (SDH) activity determined using quantitative histochemistry (50, 51). SDH activity of the biopsy was determined from absorbance measurements at 660 nm using fiber type distribution and spatially averaged SDH activity, including subsarcolemmal mitochondria, of 51 ± 11 randomly selected fibers (range, 36–79) in ImageJ software (National Institutes of Health, Bethesda, MD, USA) (34, 52). SDH activity was used to calculate muscle fiber oxidative capacity ($f\dot{V}o_{2max}$, in nmol/mm^3 per second) and whole-body oxidative capacity, according to van der Zwaard *et al.* (34). Whole-body oxidative capacity was normalized to $LBM^{2/3}$.

Fiber cross-sectional area (FCSA) was determined from fiber-type distribution and manually segmented FCSA of 51 ± 11 randomly selected fibers. Fiber circularity was calculated as shown in Eq. 2:

$$\frac{4\pi \times \mathrm{FSCA}}{(\mathrm{Perimeter})^2} \quad (2)$$

and longitudinally cut fibers were excluded from analysis [*i.e.*, circularity < 0.60 in accordance with Verdijk *et al.* (53)]. Average circularity was 0.79 ± 0.03. PCSA reflects the cross-sectional area of all fibers, including interstitial space and connective tissue. An estimate of muscle fiber number of the VL was provided by dividing the PCSA (from 3D ultrasound imaging) by average FCSA. Average SDH activity was multiplied by average FCSA to obtain spatially integrated SDH (iSDH) activity.

Capillarization was assessed by staining for *Ulex europaeus* agglutinin 1 lectin (UEA-1; Vector Laboratories, Burlingame, CA, USA) (54). Sections (10 μm) were air-dried, fixed in acetone at −20°C for 15 min, blocked with 1% bovine serum album for 30 min, and incubated at room temperature for 30 min with biotinylated UEA-1 (20 μg/ml). Subsequently, sections were incubated for 30 min with Vectastain Elite ABC Kit PK-6100 (Vector Laboratories) and incubated for 30 min with red peroxidase substrate SK-4285 (Immpact Amec; Vector Laboratories). Capillaries were analyzed for capillary-to-fiber ratio (C/F), capillaries around each fiber (CAF), and capillaries per square millimeter of muscle tissue [capillary density (CD)]. Muscle fibers and capillaries were counted from 3 photomicrographs of the biopsy section. For the C/F ratio, muscle fiber fragments cut by the left and upper margins and associated capillaries were rejected and those cut by right and lower margins were included in the analysis. Longitudinally cut capillaries were counted as 1 at each muscle fiber junction (55). On average, 265 ± 95 capillaries and 94 ± 35 muscle fibers were analyzed per subject.

The [Mb] was determined by calibrated histochemistry (52, 56). Absorbance was measured at 436 nm (52). Peroxidase activity of hemoglobin was excluded from measurements. The [Mb] was obtained after calibration using gelatin sections containing known concentrations of horse myoglobin.

Analysis of histochemistry images is described in Supplemental Data S2.

Statistical analysis

Results are expressed as means ± SD. Relationships between normalized sprint and endurance performance, between ranked normalized sprint and endurance performance, and between fiber size^{-1} and fiber oxidative capacity were assessed by Deming linear-regression analysis. Perpendicular residuals to the Deming regression lines were used to quantify PO_{peak} + PO_{TT} or the combination of $FCSA^{-1}$ and $f\dot{V}o_{2max}$ (FCSA-1 was used to take into account the hyperbolic relationship between these two variables; for details see the last paragraph of the section on whole-body cycling performance). Coefficients of determination were obtained for normalized sprint, endurance, and combined sprint and endurance performance by Pearson's correlations and stepwise multiple-regression analysis. Predictors were included in the model if a significant R^2 change ($P < 0.05$) was reported. Results were considered significant if $P < 0.05$. Tendencies were also reported if $P < 0.10$.

RESULTS

Sprint and endurance performance

Table 1 shows values for sprint performance, endurance performance, and physiologic performance determinants, whereas muscle fiber histochemistry was displayed in **Fig. 1**. The relationship between sprint and endurance performance per kilogram body mass was inverse ($r = -0.44$; $P < 0.05$). An even more-pronounced inverse relationship was shown between PO_{peak} and PO_{TT} normalized to $LBM^{2/3}$ ($r = -0.66$; $P < 0.001$, Fig. 2). Normalized sprint and endurance performance largely differed among cyclists, up to 1.5-fold and 2-fold differences, respectively. Substantial variation among subjects was also observed for combined sprint and endurance performance (PO_{peak} + PO_{TT}), reflected by perpendicular residuals. The cyclist with the highest PO_{peak} + PO_{TT} was an Olympic track cyclist competing at the highest performance level. These results indicate that the observed variation in combined sprint and endurance performance allows further exploration of critical determinants of physical performance.

Determinants of normalized sprint performance

We assessed how physiologic determinants contribute to the explained variance in normalized sprint performance (**Fig. 3**). Normalized sprint performance was explained by VL muscle volume, percentage of fast-type fibers, PCSA, blood lactate concentration, and KE maximal torque. Focusing on muscle architecture, track sprinters revealed different arrangements of their PCSA and L_f compared with the other cyclists: sprinters had a relatively large PCSA (82 ± 14 cm^2) compared with team pursuit and road cyclists (58 ± 9 cm^2), whereas their fascicle lengths were similar (9.6 ± 1.3 and 10.1 ± 1.7 cm, respectively). A large PCSA tended to be associated with large pennation angles ($r = 0.34$; $P = 0.08$), whereas a long L_f was associated with relatively small pennation angles ($r = -0.46$; $P < 0.05$). PCSA was related to FCSA of both type I and II fibers ($r = 0.56$, $P < 0.01$; and $r = 0.74$, $P < 0.001$, respectively). In the subgroup of team pursuit and road cyclists, L_f and specific force also significantly contributed to normalized sprint performance. Multiple-regression analyses showed that the percentage of

TABLE 1. *Determinants of sprint performance and endurance performance*

Determinant	All	Road cyclists		Team pursuit	Track sprinters	Range
		Amateur	International			
Whole-body						
PO_{TT} (W)	344 ± 52	316 ± 20	363 ± 39	376 ± 45	291 ± 47	233–431
PO_{peak} (W)	1327 ± 197	1380 ± 89	1203 ± 147	1256 ± 151	1592 ± 95	993–1685
Performance $\dot{V}o$ (L/min)	4.29 ± 0.52	4.03 ± 0.15	4.49 ± 0.38	4.54 ± 0.56	3.80 ± 0.48	3.09–5.45
$\dot{V}o_{2max}$ (L/min)	4.81 ± 0.43	4.52 ± 0.23	4.99 ± 0.37	4.93 ± 0.53	4.53 ± 0.27	4.11–5.65
$\dot{V}o_{2LT1}$ (L/min)	3.48 ± 0.57	3.25 ± 0.38	3.54 ± 0.46	3.68 ± 0.77	3.26 ± 0.55	2.57–4.82
$\dot{V}o_{2VT1}$ (L/min)	3.64 ± 0.41	3.28 ± 0.11	3.66 ± 0.18	3.98 ± 0.50	3.39 ± 0.33	2.93–4.53
$\dot{V}o_{2LT2}$ (L/min)	4.18 ± 0.51	3.79 ± 0.39	4.32 ± 0.37	4.43 ± 0.56	3.89 ± 0.52	3.08–5.32
$\dot{V}o_{2VT2}$ (L/min)	4.19 ± 0.45	3.87 ± 0.09	4.29 ± 0.42	4.44 ± 0.50	3.91 ± 0.34	3.34–5.13
W_{max} (W)[a]	399 ± 44	357 ± 29	408 ± 35	428 ± 48	373 ± 25	322–492
Gross efficiency (%)	21.9 ± 1.0	20.7 ± 0.2	22.4 ± 0.8	22.2 ± 1.1	21.5 ± 0.7	20.2–24.1
Muscle						
[O_2HbMb] (AU)	−13.3 ± 6.2	−13.7 ± 2.9	−14.4 ± 7.7	−12.7 ± 6.6	−12.0 ± 5.3	−31.0 to −2.6
[HHbMb] (AU)	14.5 ± 7.6	19.5 ± 14.7	14.0 ± 7.1	14.7 ± 5.2	11.6 ± 4.7	5.3–39.0
KE_{torque} (N · m)	301 ± 56	310 ± 28	294 ± 44	284 ± 72	329 ± 64	202–447
Specific force (N · cm^2)	35.4 ± 7.9	42.5 ± 6.3	37.6 ± 6.1	33.1 ± 8.5	29.9 ± 7.2	21.8–49.5
Volume (cm^3)	625 ± 136	573 ± 62	545 ± 81	631 ± 151	787 ± 88	404–892
PCSA (cm^2)	63.4 ± 14.1	53.0 ± 7.3	57.1 ± 10.2	62.3 ± 7.1	82.3 ± 13.6	46.1–97.1
L_f (cm)	10.0 ± 1.7	10.9 ± 0.5	9.6 ± 1.2	10.2 ± 2.6	9.6 ± 1.3	7.6–14.3
Pennation angle (deg)	15.5 ± 3.3	14.3 ± 2.9	15.0 ± 3.5	14.9 ± 2.4	18.0 ± 3.8	10.7–22.4
Blood						
$[Lactate]_{postWingate}$ (mM)	14.9 ± 2.7	14.2 ± 2.0	13.2 ± 2.7	15.8 ± 2.0	17.1 ± 1.9	9.3–19.6
$[Lactate]_{post\text{-}TT}$ (mM)	13.0 ± 4.1	14.7 ± 3.7	14.4 ± 2.4	13.0 ± 5.3	9.7 ± 3.7	8.0–20.3
RBC (10^{12}/L)	5.2 ± 0.4	5.3 ± 0.4	5.1 ± 0.4	5.2 ± 0.5	5.3 ± 0.5	4.4–6.2
[Hb] (mM)	9.6 ± 0.7	9.5 ± 0.9	9.7 ± 0.6	9.7 ± 0.7	9.4 ± 0.7	8.4–10.9
Hct (%)	45.8 ± 3.0	46.3 ± 3.1	45.7 ± 2.7	45.4 ± 3.2	46.3 ± 3.8	40.0–53.0
MCV (fL)	88.5 ± 2.9	87.3 ± 1.0	90.1 ± 3.0	88.3 ± 3.0	86.8 ± 2.4	83–94
MCH (amol)	1856 ± 101	1801 ± 76	1910 ± 95	1884 ± 82	1776 ± 79	1638–2091
MCHC (mM)	21.0 ± 0.7	20.6 ± 0.9	21.2 ± 0.6	21.4 ± 0.5	20.3 ± 0.4	19.7–22.3
Muscle fiber						
MHC type I (%)	67.3 ± 11.8	52.4 ± 11.2	72.1 ± 10.8	73.3 ± 7.7	61.3 ± 7.8	41.7–88.8
MHC type II (%)	32.7 ± 11.8	47.6 ± 11.2	27.9 ± 10.8	26.7 ± 7.7	38.7 ± 7.8	11.2–58.3
FCSA (μm^2)	6600 ± 1530	5847 ± 1341	6176 ± 1383	6679 ± 1725	7702 ± 1296	3354–9568
Fiber number ($\times 10^6$)	0.986 ± 0.199	0.933 ± 0.19	0.961 ± 0.23	0.976 ± 0.22	1.075 ± 0.14	0.648–1.38
$f\dot{V}o_{2max}$ (nmol/mm^3/s)	0.13 ± 0.02	0.13 ± 0.01	0.14 ± 0.02	0.14 ± 0.01	0.12 ± 0.01	0.10–0.18
Oxidative capacity (ml/kg/min)	67.2 ± 8.8	65.8 ± 6.3	70.3 ± 9.5	71.7 ± 2.9	56.7 ± 5.8	47.0–91.6
iSDH activity, ΔA_{660} (μm/s)	0.147 ± 0.034	0.131 ± 0.033	0.140 ± 0.023	0.157 ± 0.044	0.156 ± 0.035	0.093–0.229
[Mb] (mM)	0.38 ± 0.04	0.37 ± 0.05	0.39 ± 0.03	0.38 ± 0.03	0.36 ± 0.04	0.31–0.44
CD (caps · mm^2)	498 ± 97	437 ± 116	531 ± 94	546 ± 77	420 ± 49	327–769
C/F (caps/fiber)	2.9 ± 0.4	2.4 ± 0.3	2.9 ± 0.3	3.2 ± 0.5	2.8 ± 0.4	2.0–3.8
CAF (caps/fiber)	7.2 ± 1.0	6.1 ± 0.9	7.3 ± 0.8	7.9 ± 0.9	6.9 ± 0.7	5.2–9.4
[Mb] × C/F (mM · cap · $fiber^{-1}$)	1.1 ± 0.2	0.9 ± 0.2	1.2 ± 0.2	1.2 ± 0.2	1.0 ± 0.2	0.7–1.4
[Mb] × CAF (mM · cap · $fiber^{-1}$)	2.7 ± 0.5	2.2 ± 0.3	2.9 ± 0.4	3.0 ± 0.4	2.5 ± 0.3	2.0–3.7

$[Lactate]_{post\text{-}TT}$, blood lactate concentration 1 min after the time trial; $[Lactate]_{postWingate}$, blood lactate concentration 1 min after the Wingate test; oxidative capacity, whole-body oxidative capacity calculated from $f\dot{V}o_{2max}$ according to van der Zwaard *et al.* (34); performance $\dot{V}o_2$, oxygen consumption during the time trial; specific force, F/PCSA (Eq. 6.1); W_{max}, maximal work rate (3-min average during a 3-min incremental protocol, accounting for power loss within the Monark transmission system. [a]Value is expected to be lower than a W_{max} obtained from ramp or short, incremental, stepwise protocols).

fast-type fibers and VL muscle volume together explained 65% of variance in normalized PO_{peak} for the entire group, whereas 48% of the variance in normalized PO_{peak} was explained by the percentage of fast-type fibers and L_f in the subgroup of team pursuit and road cyclists. These results indicate that the major determinants of normalized sprint performance are a high percentage of fast-type fibers, large muscle volume, and long muscle fibers.

Determinants of normalized endurance performance

Normalized endurance performance was explained by gross efficiency, performance $\dot{V}o_2$, $\dot{V}o_{2max}$, $\dot{V}o_{2LT2}$, $\dot{V}o_{2VT2}$, and whole-body oxidative capacity (Fig. 3). Among blood parameters, MCH, MCHC, and MCV determined normalized PO_{TT} rather than [Hb], Hct, and RBC content. For VL parameters, the percentage

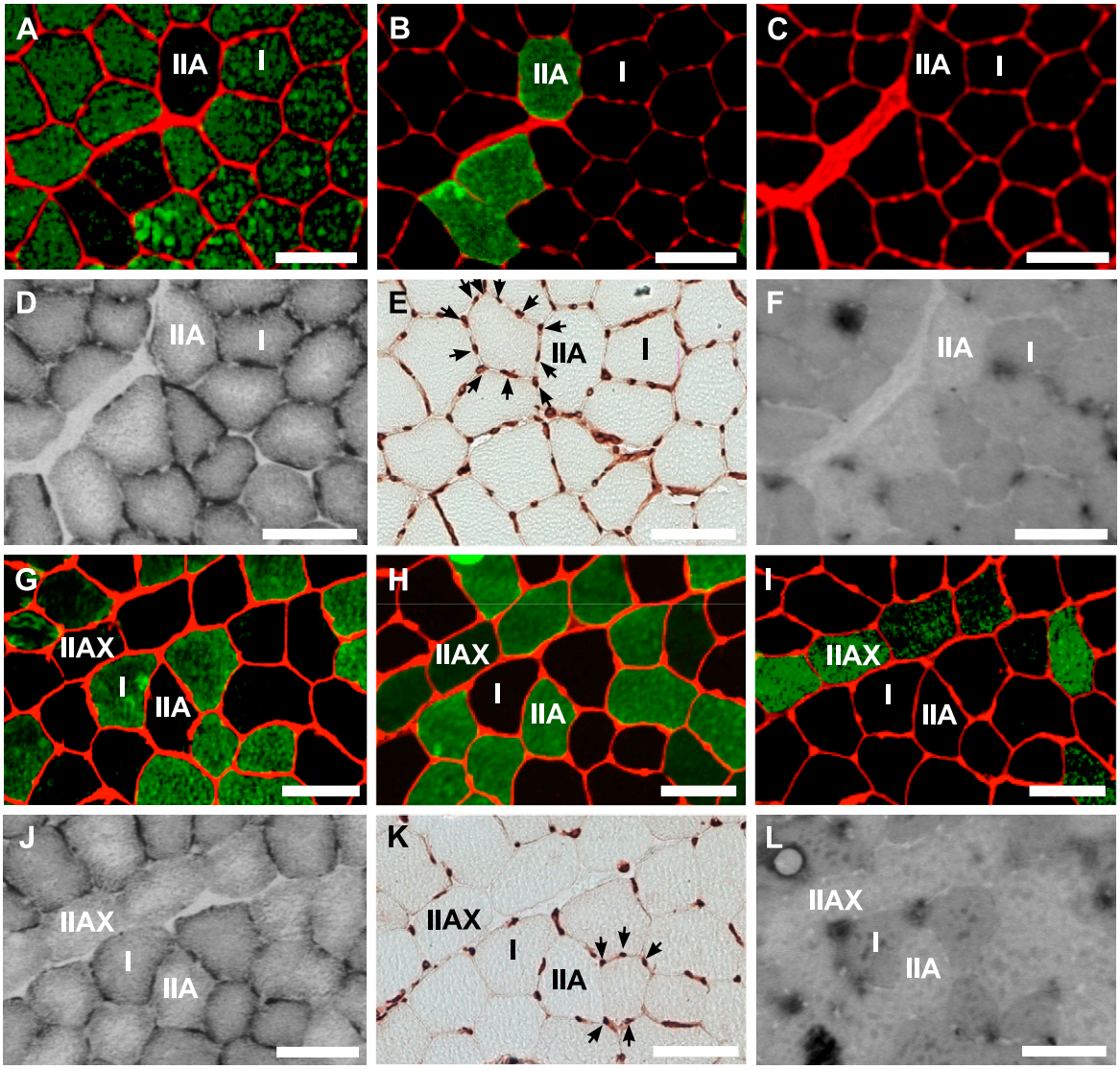

Figure 1. Immunohistochemical staining for myofibrillar MHC type I, IIA, and IIX expression (*A–C*, *G–I*) and enzyme histochemistry of SDH activity (*D*, *J*), UEA-1 lectin for capillaries (*E*, *K*), and myoglobin concentration (*F*, *L*) from an Olympic track cyclist (*A–F*) and amateur road cyclist (*G–L*), respectively. Cross sections of 10 μm were obtained from the human *musculus vastus lateralis*. Muscle fiber type I, IIA, and IIAX are identified (*A–L*); type IIX was not present in the Olympic track cyclist (*C*). Capillaries are indicated by arrows in 1 muscle fiber, indicating capillaries were more prominent in the Olympic cyclist compared with the amateur road cyclist (*E*, *K*). Histochemical assays for myoglobin (*F*, *L*) contain black spots because of peroxidase activity of hemoglobin, which was excluded from analysis. Scale bars, 100 μm.

of slow-type fibers, fiber $\dot{V}o_{2max}$, C/F, CD, CAF, and the interaction of [Mb] with C/F and CAF contributed to normalized PO_{TT}, whereas [Mb] showed a tendency ($P = 0.068$). Multiple-regression analysis revealed that performance $\dot{V}o_2$, MCHC and [O_2HbMb] together explained 92% of the variance in normalized endurance performance. Whole-body performance $\dot{V}o_2$ is a major determinant of normalized PO_{TT} and was explained by whole-body $\dot{V}o_{2max}$ and $\dot{V}o_{2LT2}$ ($R^2 = 0.93$; $P < 0.001$) or by VL parameters muscle fiber $\dot{V}o_{2max}$, the interaction of [Mb] with C/F, and PCSA ($R^2 = 0.67$; $P < 0.001$; Eq. 3). Gross efficiency was positively related to the percentage of slow-type fibers ($r = 0.45$; $P < 0.05$), C/F ($r = 0.50$; $P < 0.01$), and CAF ($r = 0.42$; $P < 0.05$). The results indicate that a high normalized-endurance performance was achieved with a high performance $\dot{V}o_2$ (*i.e.*, high muscle fiber oxidative capacity, high [Mb], many capillaries per fiber, and a small PCSA) and a high oxygen-supply capacity in the circulation (*i.e.*, MCHC and [O_2HbMb]):

$$\text{Performance } \dot{V}o_2 = 558 \times f\dot{V}o_{2max} + 103 \times [\text{Mb}] \times \text{C/F} - 0.78 \times \text{PCSA} + 117 \quad (3)$$

Determinants of combined sprint and endurance performance

$PO_{peak} + PO_{TT}$ was explained by whole-body performance $\dot{V}o_2$ and gross efficiency and showed a tendency with VL

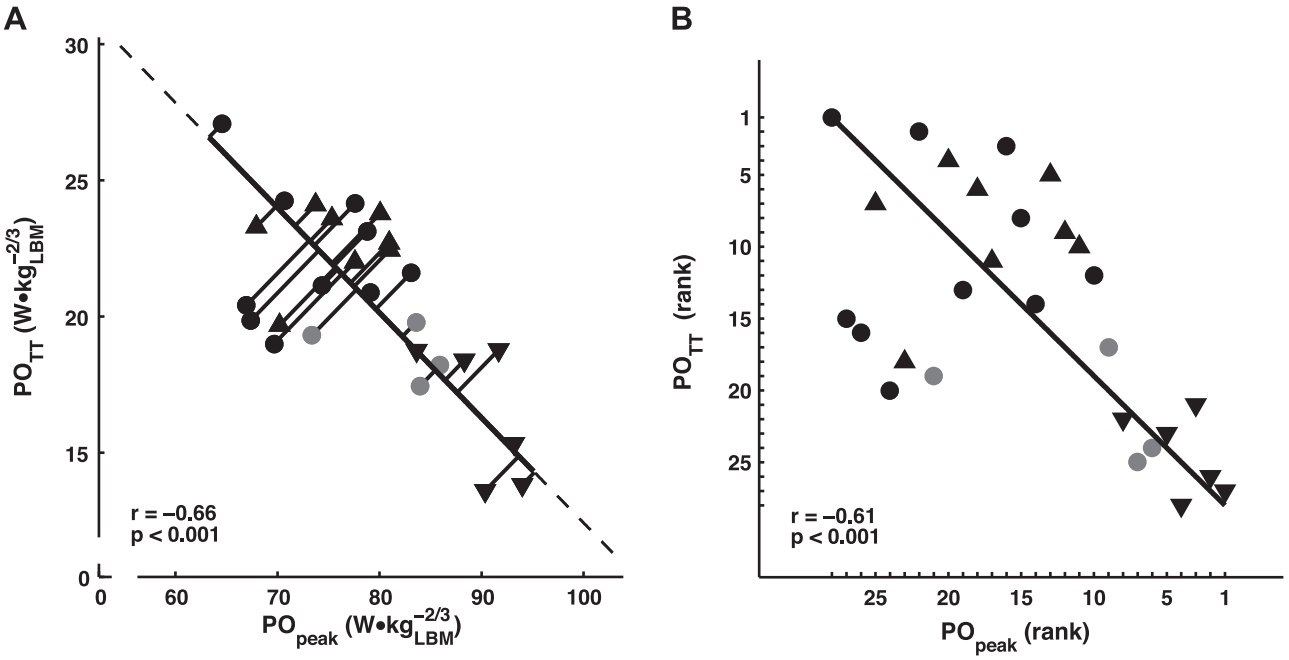

Figure 2. Normalized sprint and endurance performance are inversely related. Sprint performance (PO_{peak}) and endurance performance (PO_{TT}) were normalized to $LBM^{2/3}$. *A*) Normalized PO_{peak} and PO_{TT} demonstrated an inverse relationship ($PO_{TT} = -0.39 \times PO_{peak} + 51$), which was obtained with Deming regression analysis, accounting for errors in both variables. Individual data is provided for track sprinters (downward triangle), team pursuit cyclists (upward triangle), (inter)national road cyclists (black circle), and amateur road cyclists (gray circle). How well individual cyclists were able to combine sprint and endurance performance relative to the whole group ($PO_{TT} + PO_{peak}$) was assessed by perpendicular residuals to the regression line between PO_{TT} and PO_{peak}. These residuals quantify both how much a cyclist's sprint performance differs from his expected sprint performance (*i.e.*, δ between actual sprint performance and predicted sprint performance based on the regression line and cyclist's actual endurance performance) as well as how much endurance performance differs from his expected endurance performance (*i.e.*, δ between actual endurance performance and predicted endurance performance based on the regression line and cyclist's actual sprint performance). *B*) Ranked, normalized PO_{peak} and PO_{TT} also demonstrated an inverse relationship, as obtained with Deming regression analysis.

volume and L_f ($P = 0.056$; $P = 0.059$, respectively; Fig. 3). Arrangement of L_f and PCSA differed between track sprinters and other cyclists (as described above). Therefore, L_f may have explained less variance in $PO_{peak} + PO_{TT}$ in the whole group compared with the subgroup of team pursuit and road cyclists ($R^2 = 0.13$ and $R^2 = 0.25$, respectively). In the whole group, 30% of the variance in $PO_{peak} + PO_{TT}$ was explained by gross efficiency and VL volume. In the subgroup of team pursuit and road cyclists, 49% of the variance in $PO_{peak} + PO_{TT}$ was explained by performance $\dot{V}o_2$ and L_f.

Whole-muscle architecture may be important for $PO_{peak} + PO_{TT}$. L_f explained 13–25% of the variance in $PO_{peak} + PO_{TT}$, whereas PCSA was not related to $PO_{peak} + PO_{TT}$. Moreover, PCSA negatively affected performance $\dot{V}o_2$ (Eq. 3), which was a main determinant of combined sprint and endurance performance. These results suggest that, for VL, a long L_f, rather than a large PCSA, is likely beneficial for obtaining a high combined sprint and endurance performance.

Muscle fiber CSA and muscle fiber $\dot{V}o_{2max}$ were studied in more detail. They showed an inverse, hyperbolic relationship ($r = -0.50$; $P < 0.01$; **Fig. 4**), which illustrates that it is difficult to simultaneously obtain a large FCSA and a high muscle-fiber $\dot{V}o_{2max}$. How well the cyclists combined a large fiber size with a high oxidative capacity was assessed in absolute terms and relative to the group [*i.e.*, by the product of FCSA and f$\dot{V}o_{2max}$ (iSDH activity) and by perpendicular residuals of $FCSA^{-1}$ and f$\dot{V}o_{2max}$, respectively] (Fig. 4). It was expected theoretically that high muscle-fiber oxygen demands (*i.e.*, high iSDH activity or high residuals) were matched by enhanced oxygen-supply capacity toward and within the muscle fiber. Our results show that iSDH activity was indeed positively related to capillarization (C/F: $r = 0.58$, $P < 0.001$; CAF: $r = 0.53$, $P < 0.01$), but not to RBC, [Hb], Hct, and other blood markers ($P > 0.10$). Integrated SDH activity was not related to [Mb] ($r = -0.24$; $P = 0.23$). Similarly, perpendicular residuals of FCSA and fiber $\dot{V}o_{2max}$ were positively related to capillarization (C/F: $r = 0.57$, $P < 0.001$ and CAF: $r = 0.52$, $P < 0.01$), and showed a tendency with MCV ($r = 0.36$, $P = 0.06$), but were not related to RBC, [Hb], Hct and other blood markers ($P > 0.10$). Residuals were not related to [Mb] ($r = -0.19$; $P = 0.33$). Although fiber size and fiber oxidative capacity were inversely related, cyclists may combine a relatively large fiber size and a high oxidative capacity with enhanced capillarization.

Normalized sprint and endurance performance, as well as FCSA and f$\dot{V}o_{2max}$, were inversely related (Figs. 2 and 4). Perpendicular residuals of both regression lines were, however, not related (**Table 2**). This finding may relate to muscle fiber number because athletes with many muscle fibers have less need for combining high FCSA and f$\dot{V}o_{2max}$: muscle fiber number was negatively related to perpendicular residuals of FCSA and f$\dot{V}o_{2max}$ ($r = -0.41$; $P < 0.05$). Perpendicular residuals showed a positive

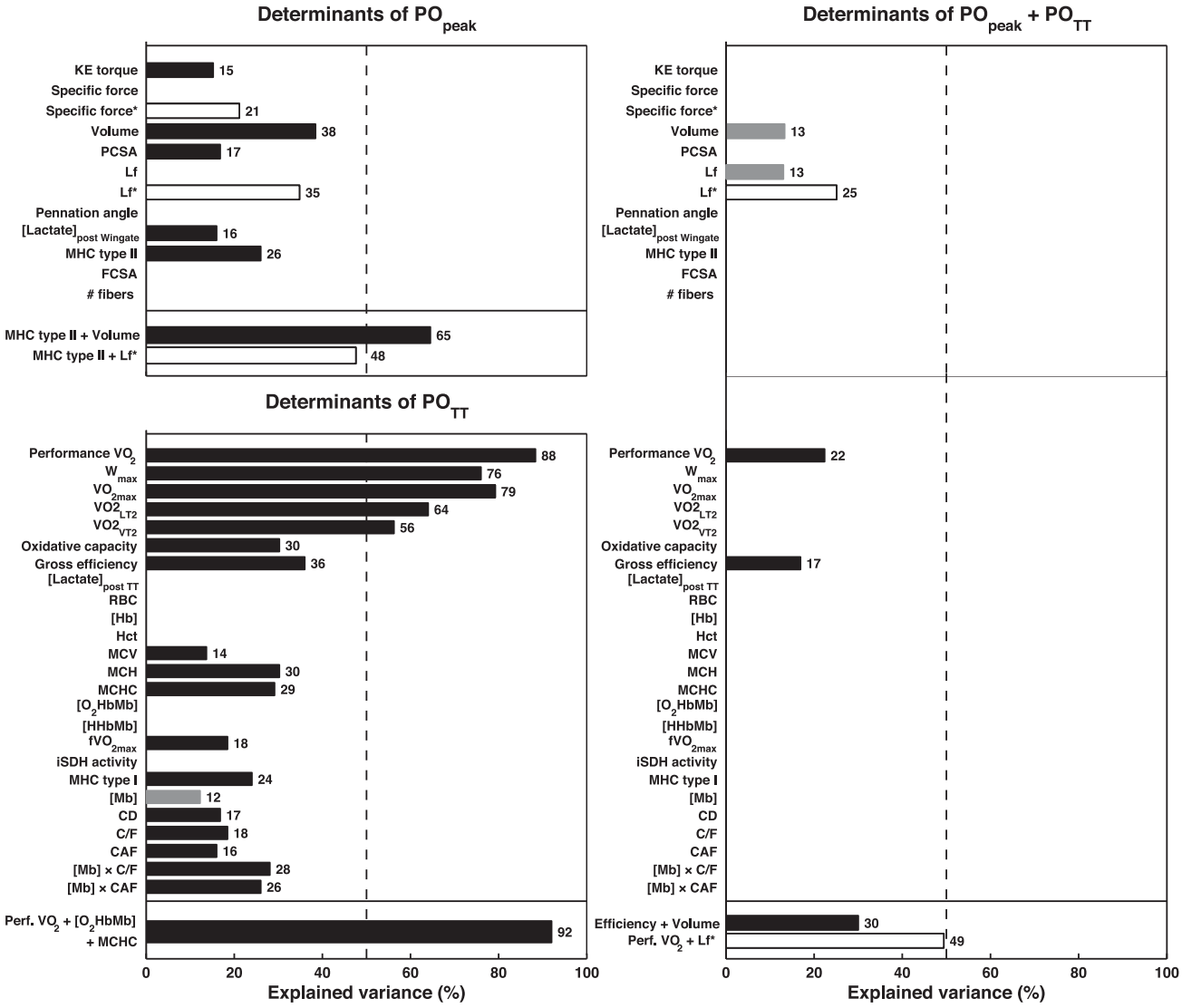

Figure 3. Determinants of normalized combined sprint and endurance performance. Sprint performance (PO_{peak}) and endurance performance (PO_{TT}) were normalized to $LBM^{2/3}$. Combined sprint and endurance performance ($PO_{peak} + PO_{TT}$) was reflected by perpendicular residuals of the regression line between PO_{peak} and PO_{TT} (Fig. 2). Bars indicate significant determinants of (combined) sprint and endurance performance in cyclists and their explained variance (% r^2) obtained from Pearson's correlations. Black bars indicate significant determinants ($P < 0.05$), and gray bars indicate a tendency ($P < 0.10$). *White bars illustrate significant determinants ($P < 0.05$) in a subgroup of team pursuit and road cyclists. Multiple-regression analyses revealed a combination of predictors, which are presented at the bottom of each panel. Whole-muscle and muscle-fiber determinants were obtained from the *musculus vastus lateralis*. Specific force, F/PCSA or KE force per physiologic cross-sectional area; $[Lactate]_{postWingate}$, blood lactate concentration 1 min after the Wingate test; MHC type II, myosin heavy chain type II proportion or proportion of fast-type fibers; # fibers, estimated muscle fiber number; $[Lactate]_{post\ TT}$, blood lactate concentration 1 min after the time trial.

relationship with endurance performance, performance $\dot{V}o_2$, $\dot{V}o_{2max}$, $\dot{V}o_2$ at lactate, and ventilatory thresholds and showed a tendency with gross efficiency (Table 2). Therefore, combining high FCSA and $f\dot{V}o_{2max}$ did not directly relate to high $PO_{peak} + PO_{TT}$, likely because of muscle fiber number but was associated with enhanced (determinants of) endurance performance.

DISCUSSION

This study integrates physiologic performance determinants at different biologic levels, from cell to whole body, to obtain insights in the critical determinants of normalized sprint, endurance, and combined sprint and endurance performance. We show that the percentage of fast-type fibers and muscle volume explain 65% of the variance in normalized sprint performance and that performance $\dot{V}o_2$ and oxygen supply within the circulation (MCHC and $[O_2HbMb]$) explain 92% of the variance in normalized endurance performance. Combined sprint and endurance performance was explained by gross efficiency, performance $\dot{V}o_2$, and likely by VL volume and L_f. The results indicate that, for VL, a long fascicle rather than a large PCSA is likely beneficial for achieving high $PO_{peak} + PO_{TT}$. Although normalized sprint and endurance performance

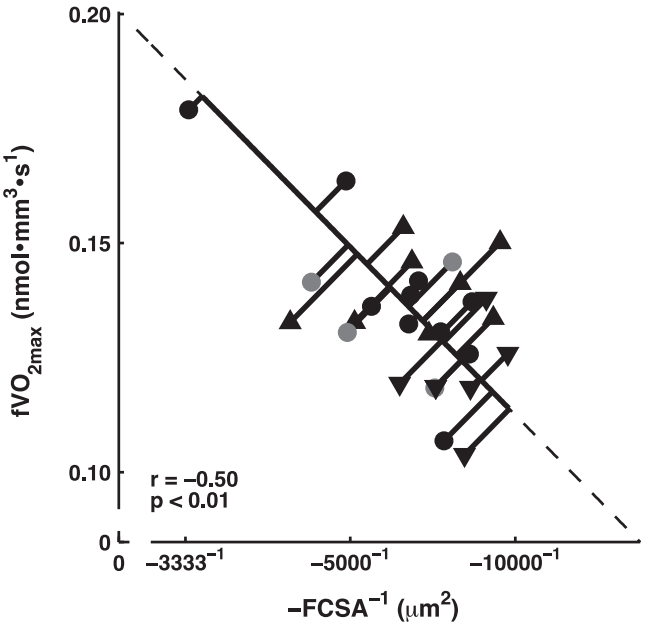

Figure 4. $f\dot{V}o_{2max}$ and FCSA demonstrate an inverse hyperbolic relationship (*i.e.*, $f\dot{V}o_{2max} = -366 \times -FCSA^{-1} + 0.076$), which was obtained with Deming regression analysis that accounts for errors in both variables. Individual data is provided for track sprinters (downward, filled triangle), team pursuit cyclists (upward, filled triangle), (inter)national road cyclists (black, filled circle), and amateur road cyclists (gray, filled circle). How well individual cyclists were able to combine $f\dot{V}o_{2max}$ and FCSA relative to the whole group was assessed by perpendicular residuals to the hyperbolic regression line between $f\dot{V}o_{2max}$ and FCSA.

as well as muscle-fiber size and muscle-fiber oxidative capacity were inversely related, cyclists succeeded at combining relatively large FCSA and high $f\dot{V}o_{2max}$ with enhanced capillarization.

Physiology of sprinters: high normalized sprint performance requires long and fast muscle fibers

We show that VL muscle volume and the percentage of fast-type fibers explain 65% of the variance in normalized PO_{peak}. That finding was not unexpected because previous data demonstrated that both muscle volume and fiber-type distribution are important for cycling peak power production (11). Peak power output during cycling could be predicted by lean body mass (16), lean leg volume (16, 30), and lean thigh volume (57). Certainly, increases in muscle mass will improve peak power production by the muscle, irrespective of its fiber-type distribution. The proportion of fast-type fibers is also critical to peak power production because it determines maximal muscle-fiber contraction velocity (27, 58, 59). Optimal pedaling velocity during sprint cycling has been shown to relate to the proportion of fast-type fibers in *musculus vastus lateralis* (30) and their proportion of the cross-sectional area (31). In line with those data, the product of lean thigh volume and optimal pedaling rate (*i.e.*, a proxy measure for fiber-type distribution) explained 83% of the variance in maximal power across the life span [from 8 to 70 yr (29)]. Although sprint performance was normalized to $LBM^{2/3}$ to remove the influence of body size, muscle volume was still a significant predictor of normalized PO_{peak}. This may indicate that large VL volume also contributes to biologic differences in power production, possibly by distributing muscle mass toward locomotory muscles or by increasing the percentage of muscle mass. The proportion of fast-type fibers is also associated with anaerobic energy production. Lactic acid production explains a large proportion of variance in sprint performance, accounting for approximately one-half of energy demands during a Wingate (60). Although blood lactate concentration was higher in our track sprinters (17.1 ± 1.9 mM) compared with team pursuit and road cyclists (14.2 ± 2.5 mM), it explained only 16% of normalized PO_{peak}, likely because it only reflects part of the total lactate production (61, 62). The results confirm that the percentage of fast-type fibers and VL muscle volume were the critical determinants of normalized sprint performance.

The question is whether VL muscle architecture influences normalized sprint performance. Arrangement of PCSA and L_f differed between the track sprinters and other cyclists, revealing a much larger PCSA but similar L_f in the track sprinters. A long fascicle length (*i.e.*, high numbers of sarcomeres in series) has theoretically been associated with high maximal muscle-fiber contraction velocity (63) and has been shown to relate to better sprint performance (14, 15). PCSA is increased by muscle-fiber hypertrophy and is thought to result in proportional increases in maximal muscle force (27, 64), assuming that specific force (F/PCSA) remains constant. However, knee-extensor specific force in our track sprinters (30 ± 7 N · cm^2) was lower than that of the other cyclists (38 ± 7 N · cm^2), and similar to that of healthy males (46). Specific force of track sprinters may have been reduced because their larger PCSAs showed a tendency toward larger pennation angles, reducing force exertion with respect to the line of pull (65). These findings may also explain why peak power per kilogram body mass of our track sprinters was lower than that of elite track sprinters [18.3 ± 1.3 W/kg compared with 19.3–20.8 W/kg (66–68)], even though absolute sprint performance was similar [1592 ± 95 W (66, 67)]. Results show that an optimal normalized sprint performance requires fast muscle fibers, a large muscle volume, and muscle architecture with long L_f rather than a large PCSA.

TABLE 2. *Relationships between perpendicular residuals of FCSA and $f\dot{V}o_{2max}$ and whole-body performance, oxygen consumption, and efficiency*

Determinant	Correlation coefficient	*P*
PO_{TT}	0.46	<0.05
PO_{peak} + PO_{TT}	0.15	0.45
Performance $\dot{V}o_2$	0.46	<0.05
$\dot{V}o_{2max}$	0.47	<0.05
$\dot{V}o_{2LT1}$	0.56	<0.01
$\dot{V}o_{2LT2}$	0.63	<0.001
$\dot{V}o_{2VT1}$	0.55	<0.01
$\dot{V}o_{2VT2}$	0.49	<0.01
Gross efficiency	0.36	0.06

Physiology of endurance cyclists: high normalized endurance performance requires high performance $\dot{V}o_2$

Normalized endurance performance was almost fully explained by performance $\dot{V}o_2$, and O_2 supply capacity in the circulation (MCHC and [O_2HbMb]). Whereas current literature predominantly reports whole-body determinants of endurance performance (1–3, 6–9, 19), we assessed how whole-body performance $\dot{V}o_2$ was explained by oxygen demand and oxygen supply within the muscle. To our knowledge, this study is the first to show that variance in performance $\dot{V}o_2$ is explained by muscle-fiber oxidative capacity, oxygen supply capacity toward and within the muscle fiber ([Mb] $\times$ C/F), and physiologic cross-sectional area of the muscle ($R^2 = 0.67$). These results suggest matching between O_2 supply and demand at the muscle-fiber level ($\dot{Q}o_2/\dot{V}o_2$ matching) and demonstrate the detrimental effect of muscle hypertrophy (*i.e.*, increase in PCSA) on average oxygen consumption during the endurance performance. The importance of $\dot{Q}o_2/\dot{V}o_2$ matching is also indicated by a higher [O_2HbMb] concentration during the time trial, reflecting lower oxygen extraction. High normalized endurance performance requires matching of O_2 demand and O_2 supply, preferably with a small PCSA.

Gross efficiency explained 36% of the variance in normalized PO_{TT} and was associated with a high percentage of slow-type fibers, similar to previous observations in competitive cyclists (69). Maximal efficiency of type I and type IIA fibers is similar (70); however, type I fibers attain their peak efficiency at lower shortening velocities (70). Accordingly, it has been suggested that a large proportion of slow-type fibers results in a higher efficiency at common cycling cadences [*i.e.*, 60−120 rpm (1)]. Gross efficiency was also associated with C/F and CAF. Note that gross efficiency was not obtained at fixed exercise intensity but at exercise intensity just below LT2 (77 $\pm$ 8% $\dot{V}o_{2max}$). When controlled for exercise intensity, partial correlation analyses show that significant correlations disappear between gross efficiency and C/F, CAF, or fiber type, suggesting that capillarization and fiber type allow steady-state O_2 consumptions at higher exercise intensities and indirectly influence gross efficiency. Future studies are warranted to investigate determinants of gross efficiency in greater detail.

Limiting factors for optimal combined sprint and endurance performance

First, we discuss findings at the muscle fiber level. Second, we discuss integration of determinants for combined sprint and endurance performance. Fiber size and fiber oxidative capacity were previously reported to be inversely related across and within animal species (25, 35). The present study shows a similar inverse hyperbolic relationship in human athletes ($r = -0.50$). Such inverse relationship between FCSA and $f\dot{V}o_{2max}$ is likely explained by matching of muscle-fiber oxygen demand and supply. Hill-type model predictions show that increases in oxygen demand (iSDH activity = FCSA $\times$ $f\dot{V}o_{2max}$) may occur, but only when accompanied by improved oxygen diffusion from capillary blood to the core of the muscle fiber (25). The oxygen diffusion depends on the solubility of oxygen in muscle, diffusion coefficient for oxygen in sarcoplasm, interstitial oxygen tension (Po_2), and the concentration of intracellular oxygen carrier Mb (71, 72). If oxygen demand exceeds oxygen supply, the muscle fiber will become hypoxic. Enhanced oxygen supply may accommodate sustained increases in oxygen demand (iSDH activity), by elevating interstitial Po_2 to prevent the center of the muscle fiber from becoming hypoxic at $\dot{V}o_{2max}$. Of note, lactic acid production from glycolytic ATP synthesis also occurs without cellular hypoxia, for instance at the start of exercise, when phosphate and ADP concentrations are low and mitochondria do not synthesize ATP at their full oxidative capacity. To our knowledge, it has never been tested whether, and to what extent, trained humans are able to increase iSDH activity values. This study shows that athletes succeeded in obtaining much greater iSDH activity values (0.147 $\pm$ 0.034 in ΔA_{660} μm/s) than untrained humans do [0.087 $\pm$ 0.004 (50)] or than patients with heart failure do [0.048 $\pm$ 0.004 (50)]. So, even though muscle fiber size and oxidative capacity were inversely related, athletes were able to obtain high iSDH activity values.

How well cyclists are able to combine relatively large FCSA with high oxidative capacity was assessed in absolute terms and relative to the group (*i.e.*, by iSDH activity and perpendicular residuals of FCSA and $f\dot{V}o_{2max}$, respectively). It was expected that high oxygen demands (high iSDH activity or high residuals) were matched by enhanced oxygen supply because of enhanced oxygen supply toward the muscle fiber, enhanced oxygen supply within the muscle fiber, relocating mitochondria to the sarcolemma (25). Firstly, our results show that iSDH activity and residuals were positively associated with capillarization (C/F and CAF) and likely with MCV, facilitating greater interstitial PO_2, reflected by higher [O_2HbMb] values. Surprisingly, both iSDH activity and residuals did not relate to RBC, [Hb], and Hct, possibly because those measures neglect differences in blood flow or blood volume (73). Secondly, [Mb] was not associated with iSDH activity or residuals ($P = 0.16$; $P = 0.23$, respectively). This could be due to the small variation in [Mb] between cyclists (coefficient of variation ~10%). Thirdly, visual inspection of staining for SDH activity indicated high subsarcolemmal SDH activities, particularly in type I fibers (Fig. 1). High combinations of muscle fiber size and fiber oxidative capacity were associated with enhanced O_2 supply toward the muscle fiber, but not within the muscle fiber.

This study shows that combined sprint and endurance performance of cyclists is associated with gross efficiency, performance $\dot{V}o_2$, and likely with VL muscle volume and fascicle length (**Fig. 5**). Performance $\dot{V}o_2$ is explained by matching of O_2 demand and O_2 supply, preferably by a small PCSA (Eq. 3). These findings illustrate that a long fascicle, rather than a large PCSA, is beneficial for achieving high PO_{peak} + PO_{TT}, thereby avoiding the inverse relationship between FCSA and $f\dot{V}o_{2max}$. Although FCSA and $f\dot{V}o_{2max}$ as well as normalized sprint and endurance performance were inversely related (Figs. 2 and 4), their residuals were not related. Both PO_{peak} + PO_{TT}

and combined FCSA and $f\dot{V}o_{2max}$ incorporate prediction errors associated with their regression line, which may explain the nonsignificant correlation. In addition, muscle fiber number was negatively related to the residuals of FCSA and $f\dot{V}o_{2max}$, suggesting that subjects with a large number of muscle fibers have less need for combining a high FCSA and $f\dot{V}o_{2max}$ to develop high combined sprint and endurance performance; they will achieve a given PCSA with smaller muscle FCSA. Muscle fiber number is determined early in life because hyperplasia does not occur in mature mammalian skeletal muscle (27, 74). Although residuals of FCSA and $f\dot{V}o_{2max}$ were not related to PO_{peak} + PO_{TT}, those residuals were associated with better endurance performance and performance $\dot{V}o_2$ and showed a tendency with gross efficiency, which are all determinants of PO_{peak} + PO_{TT}. Percentage of fast-type fibers did not determine PO_{peak} + PO_{TT}, likely because it was positively related to normalized PO_{peak} but negatively related to normalized PO_{TT}. In summary, high combined sprint and endurance performance is associated with a high gross efficiency, large muscle volume, a muscle architecture characterized by a small PCSA and long fascicles and a matching of oxidative capacity and oxygen supply capacity, preferably by well-developed capillarization.

Implications

Based on the present results, key physiologic determinants may serve as targets for training strategies in sports such as cycling to optimize sprint and endurance performance. Athletes, particularly those who need to combine high sprint and endurance, are encouraged to incorporate endurance training and resistance training that target improvement of gross efficiency, oxidative capacity and oxygen supply capacity, and muscle volume, with increases in muscle fiber length rather than muscle fiber hypertrophy. Small, but limited, increases in muscle fiber size are possible, but should be accompanied by enhanced capillarization to improve both FCSA and $f\dot{V}o_{2max}$ simultaneously.

Certainly, coaches and athletes evaluate the distance at which the athlete excels. Nevertheless, the Wingate test and time trial provide generic measures for athletes of all disciplines to assess their combined sprint and endurance performance and to characterize them within the sprint–endurance continuum. These two tests also allow time-efficient identification of new talent and help to tune those talents into their preferred sports discipline. The comprehensive physiologic profile reveals the athlete's physiologic strengths and weaknesses with respect to their sport-specific discipline, which is key to talent development, designing individualized training strategies and monitoring the progress of training interventions.

To optimize both sprint and endurance performance, future studies are warranted to investigate longitudinal effects of combined resistance and endurance training on critical physiologic determinants and physical performance. Training strategies to improve cycling efficiency may include heavy or explosive resistance training (75), but gross efficiency may also benefit from enhanced

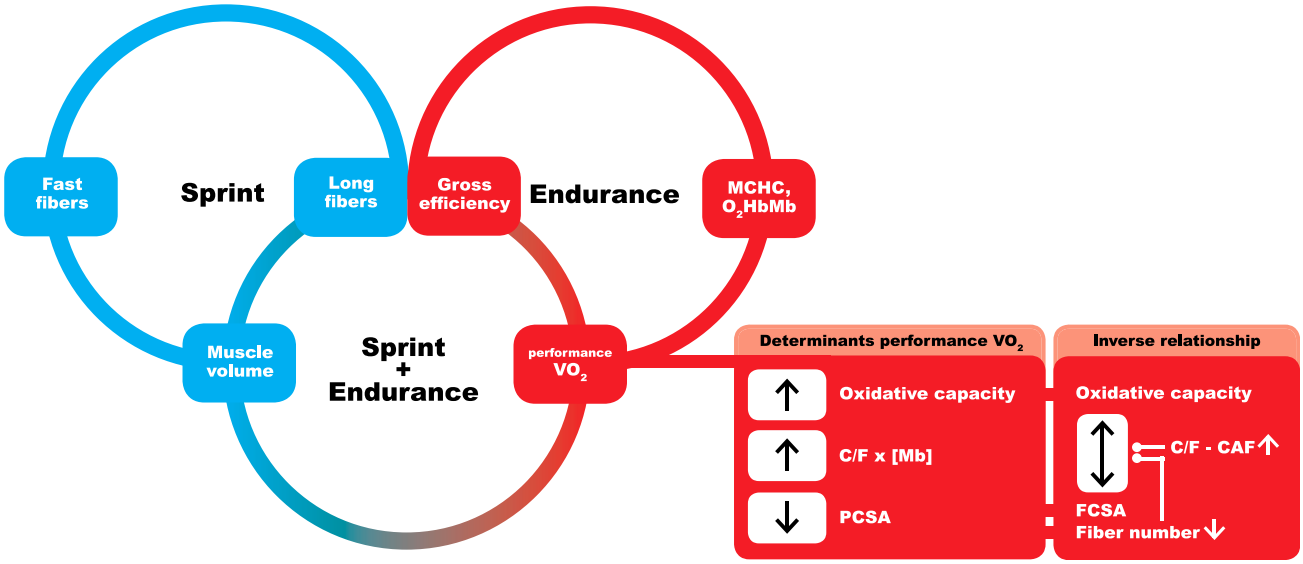

Figure 5. Physiologic determinants of normalized sprint, endurance, and combined sprint and endurance performance. Proportion of fast-type fibers, fascicle length, and VL muscle volume explain the variance in normalized sprint performance, whereas performance $\dot{V}o_2$, oxygen supply within the circulation (MCHC and [O_2HbMb]), and gross efficiency explain the variance in normalized endurance performance. Combined sprint and endurance performance was explained by gross efficiency, performance $\dot{V}o_2$, and likely, by VL volume and L_f. Performance $\dot{V}o_2$ was explained by a high muscle-fiber oxidative capacity, high oxygen-supply capacity toward and within the muscle fiber ([Mb] · C/F), and small muscle's physiologic cross-sectional area. At the muscle-fiber level, fiber size and fiber oxidative capacity were inversely related, similar to the inverse relationship between normalized sprint and endurance performance. Several cyclists succeeded in combining high FCSA and $f\dot{V}o_{2max}$ with enhanced capillarization, whereas subjects with many muscle fibers had less need for combining a high FCSA and $f\dot{V}o_{2max}$. These results suggest that fascicle length and capillarization may be important targets for individualized training strategies to optimize both sprint and endurance performance.

capillarization. Angiogenesis is induced by up-regulation of the VEGF, which occurs with exercise [for review (76)], especially during high-intensity training in hypoxic conditions (77). High-intensity training in hypoxia also increases mRNA expression of Mb (77), likely because of local tissue hypoxia within the muscle. However, hypoxia also attenuates the rate of translation and may result in muscle atrophy [for review (78)]. Endurance exercise stimulates markers for mitochondrial biogenesis, but inhibits activation of mTOR, which reduces muscle protein synthesis and muscle fiber hypertrophy (24–26). Phosphorylation of mTOR inhibits activation of myoglobin mRNA expression (79). It may be beneficial to focus on lengthening of muscle fibers (*i.e.*, the addition of sarcomeres in series), possibly with plyometric training or eccentric resistance training (80, 81). Increases in L_f enhance sprint performance, whereas it may not negatively affect $f\dot{V}o_{2max}$ necessary for a high endurance performance. Therefore, skeletal muscle adaptations for the optimal combination of both sprint and endurance performances appear to be complex and require sophisticated modulation of training intensity, timing, and mode in an individualized training strategy.

Limitations

This cross-sectional study reveals critical determinants of physical performance (Fig. 5) but did not describe longitudinal effects of resistance or endurance training on those determinants. Muscle volume arrangement into PCSA and L_f was likely suboptimal in our track sprinters and may have increased unexplained variance in performance. Additional variance may have been explained by physiologic determinants that were not measured, such as heart pumping capacity, lung diffusion and ventilation capacity, neuromuscular recruitment (*i.e.*, firing frequency, synchronization, agonist–antagonist activity), muscle metabolites [*e.g.*, phosphocreatine, muscle lactate, inosine 5′-monophosphate (IMP)], muscle tendon moment arm, tendon elasticity, or glycogen availability. Those variables may explain additional variance in combined sprint and endurance performance, whereas assessed physiologic determinants already explained a large proportion of variance in endurance and sprint performance in the present study.

CONCLUSIONS

This study integrated physiologic performance determinants from single muscle fibers to whole-body biologic levels and showed that normalized sprint performance was explained by the percentage of fast-type fibers, fascicle length, and muscle volume of the *vastus lateralis*. Performance $\dot{V}o_2$ and oxygen supply within the circulation (MCHC and [O_2HbMb]) critically determined normalized endurance performance. Combined sprint and endurance performance was explained by gross efficiency, performance $\dot{V}o_2$ (*i.e.*, high oxidative capacity, a well-developed oxygen supply capacity, and small PCSA), and likely VL volume and L_f. The results suggest that, in sports such as cycling, fascicle length and capillarization may be important training targets to optimize sprint and endurance performance simultaneously. FJ

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AUTHOR CONTRIBUTIONS

S. van der Zwaard, W. J. van der Laarse, M. J. Hofmijster, K. Levels, D. A. Noordhof, J. J. de Koning, C. J. de Ruiter, and R. T. Jaspers designed the research; S. van der Zwaard, G. Weide, and F. W. Bloemers performed the research; S. van der Zwaard, G. Weide, W. J. van der Laarse, J. J. de Koning, and R. T. Jaspers analyzed data; and S. van der Zwaard, W. J. van der Laarse, and R. T. Jaspers wrote the paper.

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